CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 64195

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 4A 2. ANDA # **64-195**

3. NAME AND ADDRESS OF APPLICANT
SangStat Medical Corporation
Attention: Hana Berger Moran (415)328-0300 ext.135
1505 Adams Drive
Menlo Park, CA 94025

4. LEGAL BASIS FOR SUBMISSION
Reference listed drug: Neoral® Oral Solution for microemulsion; Sandoz

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME SangStat SangCya®

7. NONPROPRIETARY NAME
Cyclosporine Oral Solution for microdispersion.
Note: The Division of Labeling and Program Support is considering an appropriate modifier to this name in order to differentiate it from Sandimmune®.

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

January 17, 1996	Meeting minutes.
November 21, 1996	Date of Application.
UNDATED	Labeling review deficient.
April 11, 1997	Chemistry deficient FAX.
May 20, 1997	Bio deficient letter.
April 14, 1997	T-con, chemistry.
April 29, 1997	T-con, chemistry.
July 29, 1997	T-con, labeling and front office.
August 6, 1997	Memorandum to chem from J.Phillips.
August 6, 1997	Dosing device memorandum, SangStat.
August 14, 1997	Amendment, chemistry.
August 22, 1997	Amendment, labeling.
September 2, 1997	Memorandum to file, chemistry.
March 3, 1998	Amendment.
April 14, 1998	Chemistry deficient FAX.
May 12, 1998	Amendment.
June 23, 1998	Chemistry deficient FAX.
June 30, 1998	Amendment. **This review.**

10. PHARMACOLOGICAL CATEGORY Immunosuppressive agent for the prophylaxis of organ rejection in allogeneic transplants.

11. Rx or OTC Rx

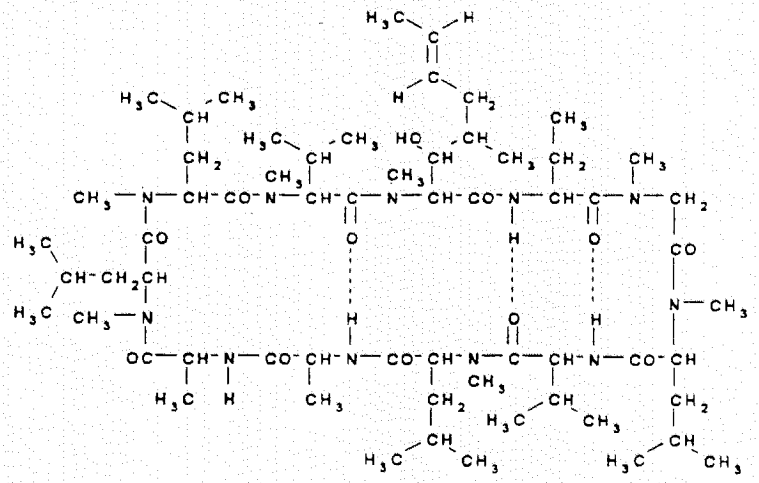
12. RELATED IND/NDA/DMF(s) See section 37. of this review.

13. DOSAGE FORM Oral Solution

14. POTENCY 100 mg/mL.

15. CHEMICAL NAME AND STRUCTURE

Cyclosporine USP; $C_{62}H_{111}N_{11}O_{12}$; M.W. = 1202.64



[R[R*,R*-(E)]]-Cyclic(L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-3-hydroxy-N,4-dimethyl-L-2-amino-6-octenoyl-L-α-aminobutyryl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl). CAS [59865-13-3]

16. RECORDS AND REPORTS N/A

17. COMMENTS

This application references Neoral® and not Sandimmune® as the reference listed drug. In terms of chemistry, the only difference between Neoral® and Sandimmune® is the formulation. Both products are solutions in bottles when they are marketed. Neoral® contains not present in the Sandimmune® formulation.

Neoral® forms a microemulsion upon mixing in water and Sandimmune® does not. The product in this application contains no oil and forms a microdispersion of solid particles upon mixing with water. The Cyclosporine Oral Solution USP monograph does not specify the character of the product after mixing with water.

Pharmaceutical Forum has recently proposed an additional monograph that would be specific for Neoral® and exclude Sandimmune®. A test to characterize the product after mixing with water will exclude Sandimmune® from the new monograph. Since the proposed monograph currently requires the formation of a microemulsion upon mixing with water it would also exclude the SangStat product, SangCya®, in this application at this time. This information has been sent to Yana Mille for inclusion with the FDA response to the USP regarding this monograph.

18. CONCLUSIONS AND RECOMMENDATIONS

Approval recommended based on CMC information.
EER pending (FUR requested); Labeling is pending.

19. REVIEWER: Jon E. Clark DATE COMPLETED: July 14, 1998